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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/834,228	04/12/2001	Elaine L. Jacobson	NIAD-214.1 US	3352

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EXAMINER

HUI, SAN MING R

ART UNIT	PAPER NUMBER
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1617

DATE MAILED: 11/20/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/834,228

Applicant(s)

JACOBSON ET AL.

Examiner

San-ming Hui

Art Unit

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-- **Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --**
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 29 August 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 30-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 30-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The cancellation of claims 17-29 in amendment filed August 29, 2002 is acknowledged. The addition of claims 30-37 in amendment filed August 29, 2002 is acknowledged.

The outstanding rejections of claims 17, 19-22, 24, 25, and 27 under 35 USC 102, first and second paragraph is withdrawn in view of the amendment filed August 29, 2002. The claims are now drawn to nicotinic acid alkyl ester wherein the alkyl ester consists of from 8 to 10 carbon atoms.

Claims 30-37 are pending.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 30-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Huber (US Patent 2,431,558).

Huber teaches topical administration of a vasodilator containing composition through skin, wherein the vasodilator may be C₄-C₈ alkyl nicotinate (i.e., butyl, pentyl, hexyl, heptyl, and octyl nicotinate) (See particularly col. 2, line 45-col.3, line 6; also claim 1). Huber also teaches that the topical administration of the alkyl nicotinate may increase the blood flow to tissue (See particularly col. 3, line 43-51).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 30 and 34-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huber (US Patent 2,431,558) in view of Otsuka et al. (US Patent 5,151,271). Otsuka is reference of record in the previous office action mailed June 18, 2002.

Huber teaches topical administration of a vasodilator containing composition wherein the vasodilator may be C₄-C₈ alkyl nicotinate (i.e., butyl, pentyl, hexyl, heptyl, and octyl nicotinate) (See particularly col. 2, line 45-col.3, line 6; also claim 1). Huber also teaches that the topical administration of the alkyl nicotinate may increase the blood flow to tissue (See particularly col. 3, line 43-51). Huber also teaches that the weight percentage of the alkyl nicotinate may be 1-10% (See particularly claim 3).

Huber does not expressly teach the method of topical administration of the octyl nicotinate composition may enhance the oxygen delivery to tissue. Huber does not expressly teach the composition comprising butyl benzoate. Huber does not expressly teach the concentration of the active as 0.1% to 1.0%.

Otsuka et al. teaches that butyl benzoate is useful as an adjuvant agent that indirectly promotes percutaneous absorption of the active in percutaneous application (See particularly col. 4, line 45-57).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate butyl benzoate into the vasodilatation method of Huber, which would increase blood flow to the tissue and increase oxygen delivery to the tissue thereby. It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate octyl nicotinate herein, in the herein claimed concentration, in the method of Huber.

One of ordinary skill in the art would have motivated to incorporate butyl benzoate into the method of Huber because butyl benzoate is known to be useful as an adjuvant agent that indirectly promotes percutaneous absorption of the active agent. Therefore, incorporate butyl benzoate into the Huber composition would have been reasonably expected to increase the absorption of any compounds of Huber, such as octyl niacin, and thereby increase its vasodilatation activity. Such vasodilatation effect and the increase of blood flow to tissue would therefore be reasonably expected to be effective to increase the delivery of oxygen to tissue. One of ordinary skill in the art would have been motivated to incorporate octyl nicotinate compounds herein in the concentration herein in the method of Huber because the optimization of result therapeutic parameters (e.g., dosage range) is obvious as being within the skill of the artisan.

It is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d

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1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, data in the instant specification, Table 2 in page 6 have been considered but are not found persuasive. The data in Table 2 merely demonstrate the duration of octyl ester is longer than that of hexyl ester. This is an expected result. This is seen to be an expected effect because the partition coefficient of octyl ester is much higher than that of hexyl ester (See Table 1 of Le et al.) No convincing and clear unexpected result is seen.

Response to Arguments

Applicant's rebuttal arguments filed August 29, 2002 averring octyl nicotinate is not tested in Huber and therefore not obvious to employ octyl nicotinate to dilating the vessels and increase the oxygen delivery thereby have been considered, but are not found persuasive. Huber clearly claims the employment of octyl nicotinate in vasodilating method therein (See claim 1). Please note that patentee is not required to exemplify every claimed compound therein. The instant claims are therefore properly rejected under 35 USC 103.

Applicant's rebuttal arguments filed August 29, 2002 averring unexpected results have been considered, but are not found persuasive because of the reasons discussed above.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

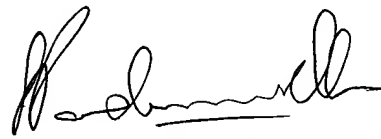
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (703) 305-1877. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

San-ming Hui
November 18, 2002



SREENI PADMANABHAN
PRIMARY EXAMINER

11/18/02